Radial glia require PDGFD-PDGFRbeta signalling in human but not mouse neocortex.

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Public Summary:

Scientific Abstract:
Evolutionary expansion of the human neocortex underlies many of our unique mental abilities. This expansion has been attributed to the increased proliferative potential of radial glia (RG; neural stem cells) and their subventricular dispersion from the periventricular niche during neocortical development. Such adaptations may have evolved through gene expression changes in RG. However, whether or how RG gene expression varies between humans and other species is unknown. Here we show that the transcriptional profiles of human and mouse neocortical RG are broadly conserved during neurogenesis, yet diverge for specific signalling pathways. By analysing differential gene co-expression relationships between the species, we demonstrate that the growth factor PDGFD is specifically expressed by RG in human, but not mouse, corticogenesis. We also show that the expression domain of PDGFRbeta, the cognate receptor for PDGFD, is evolutionarily divergent, with high expression in the germinal region of dorsal human neocortex but not in the mouse. Pharmacological inhibition of PDGFD-PDGFRbeta signalling in slice culture prevents normal cell cycle progression of neocortical RG in human, but not mouse. Conversely, injection of recombinant PDGFD or ectopic expression of constitutively active PDGFRbeta in developing mouse neocortex increases the proportion of RG and their subventricular dispersion. These findings highlight the requirement of PDGFD-PDGFRbeta signalling for human neocortical development and suggest that local production of growth factors by RG supports the expanded germinal region and progenitor heterogeneity of species with large brains.